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| APPLICATION NUMBER | FILING DATE | FIRST NAMED APPLICANT | ATTY. DOCKET NO. |
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| 09/212 | 12/18/98 | TEPPER | TEPPER-1A |

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HM12/0327

| EXAMINER | |
|---|---|
| FITZGERALD, D | |
| ART UNIT | PAPER NUMBER |
| 1646 | 6 |

DATE MAILED: 03/27/00

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

## OFFICE ACTION SUMMARY

☐ Responsive to communication(s) filed on _____

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire THREE month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

**Disposition of Claims**

☒ Claim(s) 1-23 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 1-3, 7-11, 15-17, 21, 22 is/are rejected.
☒ Claim(s) 4-6, 12-14, 18-20, 23 is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

**Application Papers**

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☒ The specification is objected to by the Examiner. (seq. rules)
☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

☒ Notice of Reference Cited, PTO-892
☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 4, 5
☐ Interview Summary, PTO-413
☒ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

☒ NOTICE... re sequences.

–SEE OFFICE ACTION ON THE FOLLOWING PAGES–

PTOL-326 (Rev. 9/00)

**1.** This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. § 1.821-1.825 for the reason(s) set forth on the attached Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures.

Applicant is requested to return a copy of the attached Notice to Comply with the response to this action.

**2.** Claims 1, 10, 22, 23, and the claims dependent therefrom are objected to because of the following informalities. Appropriate correction is required.

In all of the noted claims, "complement" is consistently misspelled.

Claim 1 additionally recites "Type IFN" at (c) where "Type I IFN" appears to be intended.

**3.** The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

**4.** Claims 10, 11, 15-17, and 21 are rejected under 35 U.S.C. § 102(b) as being anticipated by either one of Cohen *et al.*, *MCB* 15: 4208-14 (1995), or YEDA RESEARCH AND DEVELOPMENT CO., LTD. ("YEDA"), EP 0 588 177.

Each of the references describes the preparation of covalently cross-linked complexes of human IFN-α/β receptor (IFNAR2) polypeptides with IFN-α species. *See* Cohen at 4211, Fig. 3, and YEDA at 9, ll. 1-27. Additionally, the references describe binding affinity experiments in which IFN-α molecules are incubated for a time with IFNAR2 receptor preparations. Cohen at

4209, col. 2, second paragraph; and YEDA, *id.* These incubations reasonably appear to meet the limitation of "storing" the IFN, as required by claim 21.

This rejection would be obviated as to the product claims by requiring, for example, that the molecule be capable of effecting the characteristic activities (antiviral, antineoplastic, *etc.*) of the type I IFN component. Method claim 21 would be free of the present rejection if amended, *e.g.*, to require the preparation of an article of manufacture comprising a sterile formulation of the IFN·IFNAR complex.

**5.** Claims 10, 11, 15-17, 21, and 22 are rejected under 35 U.S.C. § 102(b) as being anticipated by Novick *et al.*, *J. Leukocyte Biol.* 57: 712-18 (1995).

Novick describes the purification to homogeneity of p40, a naturally occurring soluble IFNAR2 (sIFNAR2) polypeptide, its incubation with IFN-$\alpha_2$ under conditions which permit the IFN to bind to the soluble receptor, and the covalent cross-linking of the complex with DSS. Novick at 713. For the reasons discussed above with respect to the *MCB* and '177 publications, the cross-linked complexes meet the limitations of the product claims, and the incubation meets the broadest reasonable construction of the "storing" step required by claim 21. Additionally, because the p40 product described by Novick is said to be homogeneous and its incubation was conducted under conditions sufficiently similar to physiological conditions to permit the specific binding of the cytokine and the soluble receptor, it reasonably appears that the incubation mixture described by the reference would have been suitable for physiological purposes.

The exemplary amendments discussed above in connection with the § 102 rejection based on the *MCB* and YEDA '177 publications would also obviate this ground of rejection as to claims 10, 11, 15-17, and 21. This ground of rejection could be obviated with respect to claim 22 by amendment of the claim to require, *e.g.*, a pharmaceutical formulation consisting essentially of the recited IFN·IFNAR complex and a carrier or, alternatively, a unit dosage form comprising an amount of the complex suitable for administration in connection with a defined therapeutic objective.

**6.** Claims 1-3 and 7-9 are rejected under 35 U.S.C. § 103(a) as being unpatentable over either one of Novick *et al.*, U.S. Patent No. 5,821,078, or YEDA '177.

As is evident from the express limitations of dependent claim 3, all of claims 1-3 and 7-9 read on methods in which exogenous IFN and IFNAR components are administered separately to

a patient, whereby a complex is presumed to form *in vivo*. The claims require only that the amounts administered be sufficient "to provide [interferon] therapy."

Each of the references teaches that type I IFNs are known in the art as therapeutic agents for the treatment of various diseases, and that in certain of such diseases it is necessary to employ high levels of exogenous IFN to effect therapeutic benefit. Each teaches that where the levels of such exogenously administered IFN become undesirably high, soluble IFN-α/β receptor (IFNAR2) polypeptides are advantageously administered to the recipient of the therapy in order to modulate (*i.e.*, inhibit) the excess IFN. '078 at col. 13, lines 26-32; '177 at page 6, first full paragraph. Neither reference exemplifies such a method.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to administer a high level of an IFN, *e.g.*, IFN-α or -β, to a patient for a disease known in the art to be responsive to such treatment, to monitor the level of IFN activity in the patient, and to subsequently administer a soluble IFNAR2 polypeptide to the patient to modulate an undesirably high level of IFN, because each of Novick and YEDA teaches that it is desirable to do so. Because the objective of such treatment is to maintain therapeutic but non-deleterious levels of IFN, the therapies suggested by the prior art would necessarily meet the limitation of employing amounts of IFN and sIFNAR "effective to provide [interferon] therapy." The claimed invention would have been *prima facie* obvious as a whole at the time it was made, especially in the absence of evidence to the contrary.

This ground of rejection would be obviated, for example, by adding a limitation requiring that the IFN and IFNAR agents be employed in amounts such that the therapeutic efficacy of the IFN is potentiated relative to that which would be obtained with the same amount of IFN in the absence of the IFNAR.

**7.** No claim is allowed.

Claim 23 is objected to because of the informalities noted above. Prior to the present invention, there was some speculation among skilled artisans that naturally occurring soluble IFN receptor polypeptides could have some modulatory function related to the regulation of IFN subtype activity *in vivo*. *See* U.S. Patent No. 5,643,749 to Revel *et al.*, particularly at the

paragraph bridging cols. 4-5.[1] However, the sense of the prior art as a whole is that soluble IFN receptors will find use as potent inhibitors of IFN activity. *See, e.g.*, Novick (*J. Leukocyte Biol.*, 1995), cited above. The prior art thus teaches away from the instantly claimed method of administering an sIFNAR polypeptide in amount effective to potentiate the activity of an IFN in a patient.

Claims 4-6, 12-14, and 18-20 are objected to as depending from rejected base claims. They would be allowable were claims 4, 5, and 12 rewritten in independent form, including all the limitations of their respective base claims. These claims are patentable over the prior art of record because none of the references fairly suggests covalently conjugating a type I IFN with a cognate receptor polypeptide in a manner which would permit reversible dissociation of the components. Moreover, because the prior art teaches that soluble IFN receptor polypeptides are inhibitors of IFN activity, as noted above, there is no plausible motivation to provide an IFN therapeutic to a patient concurrently with such a receptor polypeptide.

**8.** Any inquiry concerning this communication should be directed to David Fitzgerald, who can be reached by any of the following means:

| | |
|---|---|
| Telephone | (703) 308-3934 |
| Fax | |
| All formal papers | (703) 308-4242 |
| Informal communications | (703) 308-0294 |
| e-mail (note PTO policies below) | david.fitzgerald@uspto.gov |

Inquiries of a general nature should be directed to the Technology Center 1600 receptionists at (703) 308-0196.

DAVID L. FITZGERALD
PRIMARY EXAMINER
ART UNIT 1646

24 March 2000

[1] Revel '749 is cited as being of interest to the present disclosure.

The **best time to reach Examiner Fitzgerald** is from 9 a.m. to 4 p.m. (Eastern). If he cannot take a call, a message may be left on his voicemail. Should attempts to reach him be unsuccessful, the supervisor for this Art Unit, Gary Kunz, may be reached at (703) 308-4623.

Most official papers and all informal **communications may be submitted to the PTO by fax.** For specific policies, refer to 37 C.F.R. § 1.6 and the notice published at 1096 O.G. 30. To facilitate their receipt and handling, please —

- Call the examiner when you send an urgent communication.
- **Do not send a duplicate copy** by mail or courier.

Any Internet **e-mail communications will be made of record in the application file**. PTO employees cannot engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. § 122. This policy is more fully set forth in the Interim Internet Usage Policy published in the PTO's *Official Gazette* on 25 February 1997 at 1195 O.G. 89.

# NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. §§ 1.821-1.825 for the following reason(s):

[ ] 1. This application clearly fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990, and at 55 FR 18230, May 1, 1990.

[ ] 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. § 1.821(c).

[X] 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. § 1.821(e).

[ ] 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. §§ 1.822 and/or 1.823, as indicated on the attached copy of the marked-up "Raw Sequence Listing".

[ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A substitute computer readable form must be submitted as required by 37 C.F.R. § 1.825(d).

[ ] 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. § 1.821(e).

[ ] 7. Other:

**Applicant must provide:**

[X] An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

[X] An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

[X] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. § 1.821(e) or § 1.821(f) or § 1.821(g) or § 1.825(b) or § 1.825(d).

For questions regarding compliance with these requirements, please contact one of the following:

For rules interpretation, call (703) 308-4216.
For CRF submission help, call (703) 308-4212.
For PatentIn software help, call (703) 557-0400.

**Please return a copy of this notice with your response.**